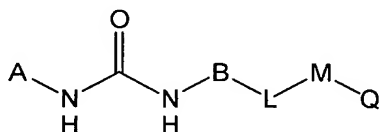


Remarks

All examined claims (claims 1-7, 19-25, 29 and 30) stand rejected under 35 USC 112, first paragraph, based on the allegations that the specification is not enabling for using the compounds of Formula 1.

Applicants assume the examiner has found no deficiency in the specification with respect to synthesizing the full scope of ureas of formula 1 in that the synthesis of the urea compounds is described generally on pages 22-26 and in the examples.

Applicants disagree with the examiners conclusion that "it is virtually impossible to determine the full scope and complete meaning of the claimed subject matter." The compounds claimed are ureas of the formula 1 below or a pharmaceutically acceptable salt thereof.



In the broadest claim (claim 1) there are 31 groups defined for aryl/hetaryl moiety A, three groups for aryl/hetaryl moiety B, 8 structures for bridging group L, and one group (pyridine) for moiety M. This extrapolates to 744 base structures which are substituted by "Q" and optionally, more conventional substituents. All of these structures are linked in that they comprise aryl/hetaryl ureas with three cyclic groups substituted by "Q".

In claim 19, the definitions for A, B, L and M extrapolate to 64 substituted urea structures of claim 1. In claim 4 the definitions for A, B, L and M extrapolate to 8 substituted urea structures of claim 1. In claim 23, the definitions for, A, B, L and M extrapolate to 4 substituted urea structures of claim 1.

When considering the substituent Q and optional substituents, claim 1 does encompass thousands of compounds, but it is not "virtually impossible to determine its scope." There are 10 groups of optional substituents for B and M (alkyl, haloalkyl, alkoxy, amino, alkylamino, dialkylamino, hydroxy, oxide, halogen and nitro); and 12 groups of optional substituents for A (R^1 , OR^1 , $S(O)_pR^1$, $C(O)R^1$, $C(O)OR^1$, $C(O)NR^1R^2$, halogen, hydroxy, oxide, amino, cyano, or nitro). The structures and groups for these substituents have clear, finite definitions such that they do not

render the scope and meaning of claim 1 and all other examined claims unclear. In addition, they are not so substantial as to change the identity of the compounds of formula I as aryl/hetaryl ureas substituted by "Q."

The substituent Q is defined as 10 structures. While these ten structures define a large number of compounds, they are structurally linked in that each has "Q" bound to a pyridine ring (M). In addition, there are structural similarities in each substituent defined by "Q." Each is bound to the pyridine group (M) via an unsaturated carbon atom which is also bound to hetero atoms (N, S and/or O). Based on these structural similarities between the claimed compounds, there is no basis to doubt the compounds claimed have similar activity. In addition, based on structural similarities with the substituents disclosed in WO 00/42012, there is no basis to doubt the compounds claimed are active in treating hyper-proliferative disorders.

As discussed in the previous response, methods for preparing pharmaceutical compositions with these compounds and methods for administering pharmaceutical compositions with these compounds in the treatment of patients are provided on pages 27-38. Here the specification discloses that the compounds claimed are suitable for treating hyper-proliferative disorders. The treatment of specific hyper-proliferative disorders is described on pages 38-40.

Assays for evaluating compounds for the treatment of these hyper-proliferative disorders were well known to those skilled in the art at the time of the invention. An example is the raf kinase assay described in application WO 00/42012, incorporated by reference on page 25.

As such, it would not be undue experimentation to test these compounds for the activity disclosed in the specification. Such testing is routine, performed on a day to day basis by those skilled in the art. The disclosure within the specification is sufficiently enabling for one skilled in the art to use any of the compounds claimed for the treatment of hyper proliferative disorders, particularly considering the advances state of the art in treating such disorders at the time of the invention.

It is alleged in the office action that "[there] is no enabling disclosure that any dose of these compounds do anything." and that "Compounds of such structural difference would not be expected to have similar utilities absent evidence to the contrary." No evidence has been presented to support these allegations as is

required to maintain a viable rejection under 35 USC §112, first paragraph, see *In re Marzocchi*, 439, F. 2d 220, 169 USPQ 367 (CCPA 1971).

In copending application 10/798,446, assigned to the same assignee as the present invention, the Board of Patent Appeals and Interferences, citing *In re Marzocchi*, reversed a rejection of claims to compounds as non-enabled (see attached Exhibit A).

The board noted on page 6 of the decision, "the PTO bears an initial burden of setting forth a reasonable explanation as to why it believes that the scope of protection provided by the claim is not adequately enabled by the description of the invention provided in the specification of the application." *Wright*, 999 F.2d at 1561-62. [T]his includes, of course, providing sufficient reasons for doubting any assertions in the specification as to the scope of enablement."

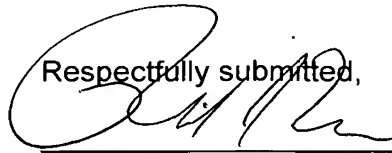
The specification in copending application 10/798,446 provides similar disclosure to that in this application with regard to preparing pharmaceutical compositions (including dosages) with the claimed compounds and administering these pharmaceutical compositions. An in-vitro assay and cellular assay are described in copending application 10/798,446. These assays were publicly disclosed at the time of filing this application in WO 00/42012 which is mentioned on page 25 of this application and incorporated by reference in this application on page 25. These assays could be routinely used to test the compounds claimed herein.

While the compounds and other facts at issue in copending application 10/798,446 are different, the disclosure provided to support the claims is similar to that of this application. In addition, the compounds claimed in copending application 10/798,446 were not assayed for activity. The compounds claimed herein are asserted to have utility based on ureas of similar structure known in the prior art to have such activity, such as those of WO 00/42012.

Applicants maintain the express disclosure within the specification enables the full scope of the pending claims as set forth above. Applicants also maintain these claims are further supported and enabled by the specification in view of the state of the art and the disclosures incorporated by reference in the specification.

In view of the above remarks and the absence of any supporting evidence, Applicants submit the rejection of claims 1-7, 19-25 and 29-30, under 35 USC §112, first paragraph should be withdrawn.

The Commissioner is hereby authorized to charge any fees associated with this response or credit any overpayment to Deposit Account No. 13-3402.

Respectfully submitted,


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Date: November 10, 2008

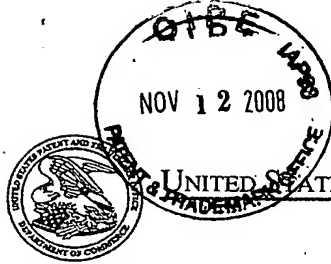


Exhibit A

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
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Alexandria, Virginia 22313-1450
www.uspto.gov

SEP 25 2008

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/071,248	02/11/2002	Bernd Riedl	BAYER-15_P4	9631

23599 7590 09/23/2008
MILLEN, WHITE, ZELANO & BRANIGAN, P.C.
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ARLINGTON, VA 22201

ACTION

DUE DATE

Reg Recn / Cmt / CAFE
11/23/08

EXAMINER

DESAI, RITA J

ART UNIT

PAPER NUMBER

1625

MAIL DATE

DELIVERY MODE

09/23/2008

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

ACTION _____

DUE DATE _____

OK'd
9/25/08

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte

BERND RIEDL, JACQUES DUMAS, UDAY KHIRE,
TIMOTHY B. LOWINGER, WILLIAM J. SCOTT,
ROGER A. SMITH, and JILL E. WOOD

Appeal 2008-3178
Application 10/071,248
Technology Center 1600

Decided: September 23, 2008

Before DONALD E. ADAMS, ERIC GRIMES, and MELANIE L.
McCOLLUM, *Administrative Patent Judges*.

McCOLLUM, *Administrative Patent Judge*.

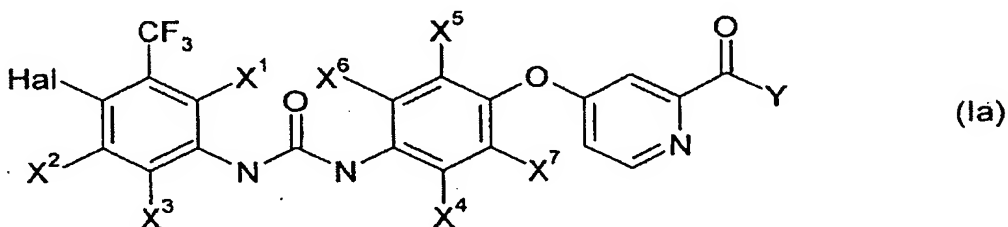
DECISION ON APPEAL

This is an appeal under 35 U.S.C. § 134 involving claims to a compound and a treatment method administering the compound. The Examiner has rejected the claims as nonenabled. We have jurisdiction under 35 U.S.C. § 6(b). We affirm-in-part.

STATEMENT OF THE CASE

Claims 1-15 and 22 are pending and on appeal. We will focus on claims 1 and 22, which are representative and read as follows:

1. A compound of formula (Ia)



wherein,

Y is NHR,

Hal is chlorine or bromine,

R is H, CH₃ or CH₂OH, and

X¹ to X⁷ are each, independently, H, OH or -OC(O)C₁-C₄ alkyl, or a salt or purified stereoisomer thereof,

with the proviso that at least one of X¹ to X⁷ is OH or -OC(O)C₁-C₄ alkyl.

22. A method of treating osteoporosis and inflammation, in a mammal by administering an effective amount of a compound of claim 1.

Claims 1-15 and 22 stand rejected under 35 U.S.C. § 112, first paragraph, "because the specification, while being enabling for using compounds which do not have to have a OH or an -OC(O)C₁-C₄ []alkyl, does not reasonably provide enablement for compounds that do have . . .

them and also [does not reasonably provide enablement] for treating osteoporosis and inflammation” (Ans. 3).¹

Appellants contend that the Examiner erred in concluding that the claims are not enabled.

ISSUES

The issues are whether the Examiner has set forth a prima facie case that the compounds of claim 1 and the method of claim 22 are not enabled and, if so, whether Appellants have rebutted the Examiner’s prima facie case.

FINDINGS OF FACT

1. The Specification states that the “invention provides compounds which are inhibitors of the enzyme raf kinase” (Spec. 2: 5).
2. The Specification states that such compounds “are useful in pharmaceutical compositions for human or veterinary use where inhibition of the raf kinase pathway is indicated, e.g., in the treatment of tumors and/or cancerous cell growth mediated by raf kinase” (*id.* at 2: 6-9).
3. In particular, the Specification discloses compounds of Formula I (*id.* at 2: 20 to 5: 3).
4. The Specification states that “[p]reference is given to a compound of formula (Ia)” (*id.* at 6: 9-22), which is a subset of compounds within Formula I and is the formula recited in claim 1.

¹ In a communication mailed November 20, 2007, the Examiner provides a response to the Reply Brief. In view of the February 19, 2008, Order Returning Undocketed Appeal to the Examiner and the subsequent issuance of the March 3, 2008, communication noting entry of the Reply Brief, it is understood that the November 20, 2007, communication has been vacated.

5. The Specification states that the “compounds of Formula I may be prepared by the use of known chemical reactions and procedures” (*id.* at 15: 14-15).

6. Nevertheless, the Specification provides “general preparative methods” (*id.* at 15: 15 to 19: 3).

7. The Specification states that the “compounds may be administered orally, topically, parenterally, by inhalation or spray or rectally in dosage unit formulations” (*id.* at 19: 8-9).

8. The Specification discloses administering a daily dosage of 0.1 to 200 mg/kg of total body weight (*id.* at 21: 28-32).

9. The Specification also states that the “activity of a given compound to inhibit raf kinase can be routinely assayed, e.g., according to procedures disclosed below” (*id.* at 22: 27-28).

10. The Specification includes Examples disclosing the synthesis of 103 compounds (*id.* at 23-84). The Specification states that compounds that have been synthesized are listed in the Tables (*id.* at 84: 13-14). Tables 1-6 depict 103 compounds (*id.* at 85-97).

11. The Examiner finds and Appellants do not dispute that none of these specifically disclosed compounds are within formula (Ia) of claim 1 (Ans. 4-5).

12. However, among these compounds, the Specification discloses compounds, specifically Compounds 42, 43, and 85, that differ from Formula (Ia) of claim 1 only in that the compounds do not meet the proviso that “at least one of X¹ to X⁷ is OH or -OC(O)C₁-C₄ alkyl” (Spec. 89-90 & 94-95).

13. The Specification also discloses using a p38 kinase inhibition assay to determine the *in vitro* inhibitory properties of compounds (*id.* at 97: 7-9). The Specification states that “[a]ll compounds exemplified displayed p38 IC₅₀s of between 1 nM and 10 μM” (*id.* at 98: 1).

14. The Specification does not mention the terms “osteoporosis” and “inflammation” except in claim 22.

ANALYSIS

“[T]o be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without ‘undue experimentation.’” *In re Wright*, 999 F.2d 1557, 1561 (Fed. Cir. 1993).

[A] specification disclosure which contains a teaching of the manner and process of making and using the invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented *must* be taken as in compliance with the enabling requirement of the first paragraph of § 112 *unless* there is reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support.

In re Marzocchi, 439 F.2d 220, 223 (CCPA 1971) (emphasis in original).

“It is well settled that patent applicants are not required to disclose every species encompassed by their claims, even in an unpredictable art.” *In re Vaeck*, 947 F.2d 488, 496 (Fed. Cir. 1991). “[S]ufficient disclosure . . . to teach those of ordinary skill how to make and how to use the invention . . . means that the disclosure must adequately guide the art worker to determine, without undue experimentation, which species among all those encompassed by the claimed genus possess the disclosed utility.” *Id.*

“When rejecting a claim under the enablement requirement of section 112, the PTO bears an initial burden of setting forth a reasonable explanation as to why it believes that the scope of protection provided by that claim is not adequately enabled by the description of the invention provided in the specification of the application.” *Wright*, 999 F.2d at 1561-62. “[T]his includes, of course, providing sufficient reasons for doubting any assertions in the specification as to the scope of enablement. If the PTO meets this burden, the burden then shifts to the applicant to provide suitable proofs indicating that the specification is indeed enabling.” *Id.* at 1562.

Claim 1 is directed to a compound within formula (Ia). The Specification states that compounds described therein “are inhibitors of the enzyme raf kinase” and “are useful . . . in the treatment of tumors and/or cancerous cell growth mediated by raf kinase” (Findings of Fact (FF) 1-2). The Examiner has not set forth sufficient basis to doubt that the compounds of claim 1 would be useful for this purpose.

The Examiner argues:

The state of the prior art is that the drugs and the enzymes react in a lock and key mechanism and the structure of the compound has to be specific. Even a difference of a methyl group verses [sic] a hydrogen changes the properties altogether. A good example is a theophylline verses [sic] caffeine. They differ by just a methyl group but one of them has a pharmaceutical use as a bronchodilator. There is no absolute predictability and no established correlation between the different substitutions on a core that they would all behave in the exact same way. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic regimen on its face.

(Ans. 3-4.)

We are not persuaded. Although we agree that this art is not absolutely predictable and that even a difference of a methyl group may in some circumstances change the properties of a compound, we do not agree that this argument alone is sufficient to provide a prima facie case that claim 1 is not enabled. The Examiner has not set forth a sufficient case that the compounds of claim 1 lack any disclosed utility, nor has the Examiner set forth a prima facie case that one of ordinary skill in the art would not have been able to use the compounds without undue experimentation. Instead, the Examiner focuses on whether the Specification provides sufficient guidance for treating osteoporosis and inflammation (Ans. 7-17). However, claim 1 does not require the treatment of osteoporosis or inflammation.

In addition, we do not agree that the Examiner has set forth a prima facie case that one of ordinary skill in the art would not have been able to make the compounds of claim 1 without undue experimentation. In particular, the Specification provides disclosure of the synthesis of structurally similar compounds (FF 5-6 & 10). The Examiner has not explained why one of ordinary skill in the art would not have been able to make the compounds of claim 1 based on this disclosure. In fact, at one point, the Examiner states that she "has not raised the issue of how to make the compounds" (Ans. 6).

For these reasons, we reverse the enablement rejection of claim 1. For the same reasons, we also reverse the enablement rejection of compound claims 2-15.

In contrast, claim 22 is directed to a method of treating osteoporosis and inflammation. As noted by the Examiner, the Specification “has no guidance to treating inflammation and osteoporosis” (Ans. 3). In fact, the Specification does not even mention the terms “osteoporosis” and “inflammation” except in claim 22 (FF 14). We agree that the Examiner has set forth a prima facie case that the Specification does not enable claim 22.

Appellants argue, however, “that one skilled in the art could perform the methods defined in claim 22 based on the disclosure within the specification and what was known in the art at the time of filing the application, particularly in view of the disclosure of p38 inhibition by structurally related compounds” (App. Br. 6). In particular, relying on WO 98/52558, which is of record in this application but was not listed in the Evidence Appendix included with the Appeal Brief, Appellants argue that it is “recognized in the art that inhibitors of p38 will be effective in treating osteoporosis and inflammation” (*id.* at 4).

In addition, Appellants argue that the Specification “provides disclosure that structurally related compounds inhibit p38. Because some of these structurally related compounds vary from those of formula Ia only in the required OH or -OC(O)C₁-C₄ alkyl substituents, while varying significantly from each other, it is not objectively doubttable that the compounds of formula Ia also inhibit p38 in a manner consistent with the exemplified compounds.” (*Id.* at 6-7.) In addition, “[g]iven this disclosure within the specification and the nexus between p38 inhibitors and the treatment of osteoporosis and inflammation known in the art, it would at most involve routine experimentation if any at all, for one of ordinary skill

in the art to treat osteoporosis or inflammation with a compound of formula Ia” (*id.* at 7).

We are not persuaded. As noted by the Examiner, “a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion.” *Genentech, Inc. v. Novo Nordisk A/S*, 108 F.3d 1361, 1366 (Fed. Cir. 1997) (quoting *Brenner v. Manson*, 383 U.S. 519, 536 (1966)).

Patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable. . . . Tossing out the mere germ of an idea does not constitute enabling disclosure. While every aspect of a generic claim certainly need not have been carried out by an inventor, or exemplified in the specification, reasonable detail must be provided in order to enable members of the public to understand and carry out the invention. . . .

[A] specification need not disclose what is well known in the art. However, that general, oft-repeated statement is merely a rule of supplementation, not a substitute for a basic enabling disclosure. It means that the omission of minor details does not cause a specification to fail to meet the enablement requirement. . . . It is the specification, not the knowledge of one skilled in the art, that must supply the novel aspects of an invention in order to constitute adequate enablement.

Genentech, 108 F.3d at 1366 (citation omitted).

Appellants are correct that enablement does not necessarily require an example. However, Appellants’ application only mentions osteoporosis and inflammation in the context of claim 22 (FF 14). In addition, the p38 assay relied upon by Appellants does not indicate that any of the compounds encompassed by claim 22 were tested, much less that they inhibit p38 (FF 10-11 & 13). Therefore, Appellants have not identified, nor did we find,

any recitation in the Specification that the compounds encompassed by claim 22 inhibit p38. Thus, even assuming that there was a known nexus between inhibition of p38 and osteoporosis and inflammation, we do not agree that Appellants have rebutted the prima facie case that claim 22 is nonenabled. Instead, we agree with the Examiner that, at best, Appellants' disclosure provides "vague intimations of general ideas that may or may not be workable." Therefore, we affirm the enablement rejection of claim 22.

CONCLUSION

We reverse the enablement rejection of claims 1-15. However, we affirm the enablement rejection of claim 22.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 C.F.R. § 1.136(a).

AFFIRMED-IN-PART

cdc

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